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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,160	12/11/2000	Balin Balinov	NIDN -10369	2196

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AMERSHAM BIOSCIENCES
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER

HARTLEY, MICHAEL G

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 09/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/673,160

Applicant(s)

BALINOV ET AL.

Examiner

Michael G. Hartley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

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Response to Amendment

The preliminary amendment filed 12/11/2001 has been entered. Claims 5, 8, 10, 11, 12, 15, 18 and 21 have been amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the recitation of "heterogeneous gas-containing nucleation sites" is indefinite because it is unclear what is meant or encompassed thereby. The specification fails to define this term and it is not a recognized term of art. It is unclear by the use of "nucleation" is this is only a gaseous precursor or any gas, and if it requires the presence of "gas" by "gas-containing" (or may be a gaseous precursor). Also, it is unclear what is meant by "heterogeneous" and to what the site is "heterogeneous." Thus, it is unclear what components are encompassed by "heterogeneous gas-containing nucleation sites" or what is excluded thereby.

The dependent claims fall therewith.

Claims 21 and 22 provide for the use of a contrast agent, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

Claims 21 and 22 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte*

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Dunki, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12 and 15-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Apfel (WO 97/25097).

Apfel discloses a dispersion of superheated drops in an aqueous liquid which is an oil-in-water emulsion, see abstract, page 8 and 14. The superheated drops are in oil and are gas nucleating as they vaporize by activation using ultrasound, see abstract. The drops include fluorocarbons, hexafluoropropylene, etc. (e.g., page 8) and include stabilizing membranes, such as, emulsifiers (e.g., page 9 and 23, including fatty acids), forming gas-containing microbubbles. The emulsions may further comprise a drug for methods of drug delivery and are useful in methods of ultrasound imaging, see abstract and pages 20-21.

Claims 1-12 and 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Berg (WO 94/21301).

Berg discloses an oil-in-water emulsion containing gas nucleation sites, such as, dissolved gaseous perfluorocarbons or microparticles which act as nucleation sites, see abstract page 7 and page 9, last paragraph. The perfluorocarbons include those as claimed, see page 7. The emulsions include the use of stabilizers, e.g., phospholipids, as claimed, see page 9. The emulsions are useful in methods of ultrasound imaging, see abstract and pages 20-21.

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Claims 1-12 and 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Lohrmann (US 5,716,597).

Lohrmann discloses oil-in-water emulsions which comprise a gas forming component therein which is a gas containing nucleation site (e.g., a perfluorocarbon, etc.), which is activated by ultrasound, see abstract and columns 3-4. The emulsions include various surfactants, including phospholipids, etc., see column 4-5. The emulsions are useful in methods of ultrasound imaging, see abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Apfel (WO 97/25097) or Berg (WO 94/21301) or Lohrmann (US 5,716,597) in view of Unger (WO 98/10799).

Apfel, Berg and Lohrmann disclose oil-in-water emulsions which comprise a gas forming component therein which is a gas containing nucleation site, which is activated by ultrasound, e.g., a perfluorocarbon, etc., as set forth above.

Apfel, Berg and Lohrmann fail to disclose that the compositions also include a vasodilator (i.e., adenosine) and Berg and Lohrmann fail to teach the addition of a drug.

Unger discloses ultrasound contrast agents and methods thereof and teaches that it is advantageous to add a vasodilator to such compositions to improve the imaging, which provides for detection of disease and measuring blood flow, see abstract. Unger discloses the use of adenosine as a vasodilator for improving methods of imaging, see page 71. Unger also teaches that it is well known in the art to include a therapeutic agent in such contrast agents to provide a dual diagnostic and therapeutic effect, see page 11.

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It would have to one of ordinary skill in the art to modify the compositions disclosed by any of Apfel, Berg or Lohrmann to include a vasodilator because the addition of vasodilators to contrast agent compositions is well known in the art to improve imaging of the cardiovascular region and provide effective imaging to detect disease and measure blood flow, as shown by Unger. One of ordinary skill in the art would have been motivated to add a vasodilator (i.e., adenosine) to the contrast agent compositions disclosed by Apfel, Berg or Lohrmann to gain the many advantages specifically taught by Unger. Also, it would have been to one of ordinary skill in the art to modify the compositions disclosed by either Berg or Lohrmann to include a therapeutic agent therein because it is known in the art that such contrast agent may further include a drug to provide a dual action diagnostic and therapeutic agent, as taught by Unger, as well as, Apfel.

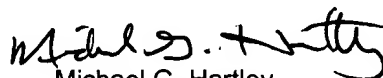
Conclusion

No claims are allowed a this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose G. Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
September 23, 2002